The impact of fluid resuscitation on the capillary leak in septic shock: Evaluation of CLI, CXCL10, cumulative fluid balance, organ dysfunction, and mortality

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Abstract

***Background*: Fluid resuscitation is a key management strategy for septic shock patients who experience increased capillary permeability. Using capillary leakage index (CLI) and C-X-C motif chemokine ligand 10 (CXCL10) biomarkers, capillary leakage can be assessed not only through hemodynamic changes but also as a distinct phenomenon. This study aimed to evaluate the relationship between resuscitation and capillary leakage in septic shock patients.**

***Methods*: This study employed an observational cross-sectional design, including 35 septic patients admitted to the Intensive Care Unit (ICU) of Dr. Wahidin Sudirohusodo Hospital. Standard sepsis management was performed, and CLI and CXCL10 levels were measured on the first and third days after sepsis diagnosis, along with cumulative fluid balance delta assessment. The study was conducted from July to November 2024.**

***Results*: The mean CLI value on the first day was 68.42±57.28, decreasing to 44.14±46.43 on the third day. The mean CXCL10 value on the first day was 47.70±45.47, decreasing to 29.34±28.12 on the third day. The mean cumulative fluid balance delta was 727.88±1538.62. CLI and CXCL10 levels on the third day showed a significant correlation with Sequential Organ Failure Assessment (SOFA) scores, whereas no correlation was found on the first day. CLI was significantly correlated with Acute Physiology And Chronic Health Evaluation (APACHE) II scores, whereas CXCL10 did not show a significant correlation with APACHE II. A significant correlation was observed between CLI, CXCL10, and cumulative fluid balance delta on the third day of treatment.**

***Conclusion*: CLI and CXCL10 can be used as biomarkers for capillary leakage to assess clinical conditions and prognosis within <72 hours. Although CXCL10 is not as strong as CLI, it can still serve as an indicator of capillary leakage in septic shock patients. Evaluating CLI and CXCL10 biomarkers on the third day is recommended for an accurate assessment of the patient's clinical condition.**

Key words: Septic shock, capillary leakage, CLI, CXCL10, SOFA score, APACHE II.

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Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection, with septic shock representing its most severe manifestation, characterized by profound circulatory and metabolic abnormalities that significantly increase mortality. Globally, sepsis and septic shock are major healthcare burdens, affecting millions annually and contributing to high mortality rates, with one in three septic patients and one in six septic shock patients succumbing to the condition. Early identification and timely management within the

first hours following diagnosis have been shown to improve outcomes. (1,2)
The mortality rate associated with sepsis is alarmingly high, surpassing that of acute coronary syndrome and stroke. Epidemiological studies from 1980 to 2008 in the United States, Brazil, the United Kingdom, and Australia reported sepsis incidence ranging from 22 to 240 per 100,000 population, severe sepsis from 13 to 300 per 100,000, and septic shock at 11 per 100,000. A local study at Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta, between 2012 and 2013 found a mortality rate of 61% among severe sepsis and septic shock patients. (1)
Septic shock results from systemic activation of inflammatory pathways involving various mediators such as cytokines, kinins, complement proteins, coagulation factors, and eicosanoids, leading to cardiovascular dysfunction and organ failure. Key mediators, including tumor necrosis factor alpha (TNFα), interleukin (IL)-1β, platelet-activating factor (PAF), and prostaglandins, play crucial roles in reducing peripheral vascular resistance, a hallmark of septic shock. Increased microvascular permeability is an early sign of endothelial injury, allowing albumin and macromolecules to extravasate into the interstitial space, resulting in hypovolemia, hemodynamic instability, and edema. (3,4)
Fluid resuscitation remains the cornerstone of treatment for endothelial dysfunction and capillary leakage in sepsis. The 2021 Surviving Sepsis Campaign (SSC) recommends administering at least 30 ml/kg of intravenous crystalloids within the first three hours of resuscitation for sepsis-induced hypoperfusion. For septic shock, norepinephrine is the first-line vasopressor to maintain a mean arterial pressure (MAP) above 65 mmHg. (2) However, excessive fluid resuscitation can lead to fluid overload, exacerbating interstitial edema, pulmonary complications, and multi-organ dysfunction, increasing morbidity and mortality. (5-8)
Several biomarkers have been explored to assess capillary leakage in sepsis, including C-X-C motif chemokine ligand 10 (CXCL10), also known as interferon gamma-induced protein 10 (IP-10). CXCL10 binds to the C-X-C motif chemokine receptor 3 (CXCR3), playing a crucial role in inflammatory responses and lymphocyte activation. Elevated CXCL10 levels have been detected in various infections, including viral, bacterial, fungal, and parasitic infections, indicating its role in sepsis pathogenesis and systemic capillary leak syndrome. (9-11) Clinical studies demonstrate that plasma CXCL10 levels correlate with sepsis severity and may predict the transition from sepsis to septic shock (11,12).
Another proposed marker, the capillary leak index (CLI), is calculated using C-reactive protein (CRP) and albumin levels to evaluate endothelial permeability and sepsis severity. (13,14) High CLI values have been associated with worse outcomes in critically ill patients (15-17). Given the critical role of endothelial dysfunction in sepsis, monitoring capillary leaks through CXCL10 and CLI may offer valuable insights for optimizing fluid resuscitation strategies. (16,18) This study aimed to assess the relationship between fluid resuscitation and capillary leakage in septic shock patients, potentially guiding better management strategies to improve outcomes.

Material and methods

Settings and design

This study employed an observational design using a cross-sectional method to examine the relationship between resuscitation and capillary leakage phenomenon in patients with septic shock. The study was conducted in the Intensive Care Unit (ICU) of Dr. Wahidin Sudirohusodo Hospital, Makassar, from June 1, 2024, until the required sample size was achieved.

Study group

The study population consisted of patients admitted to the ICU of Dr. Wahidin Sudirohusodo Hospital, Makassar. The sample included patients diagnosed with sepsis based on quick Sequential Organ Failure Assessment (qSOFA) and systemic inflammatory response syndrome (SIRS) criteria. If patients met both criteria, they were further assessed for inclusion and consented to participate in the study. A consecutive sampling method was used, wherein subjects meeting the eligibility criteria were included until the required sample size was met. This approach allowed efficient data collection while minimizing selection bias. The inclusion criteria were patients aged 18 years or older, diagnosed with sepsis, and willing to participate in the study. Exclusion criteria included pregnant women, patients with hemorrhagic shock, contraindication to administered fluids, those with chronic conditions affecting fluid balance, and patients or their families who declined participation.

Ethical considerations

Ethical clearance was obtained from the Biomedical Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (No. 413.UN4.6.4.5.31/PP36/2024). All eligible patients provided written informed consent before participation in the study.

Study protocol

Patients diagnosed with septic shock who met the study criteria were enrolled. Blood samples were collected to measure CRP and albumin levels (as the components of the capillary leakage index) and CXCL10 (C1) before resuscitation (T1). CRP and albumin were measured using Cobas Integra 400 (Roche, USA), and CXCL10 levels were measured using E-EL-H00050 (Elabsciense, USA). Fluid resuscitation was administered using a mini-fluid challenge with 100 ml of Ringer's lactate over one minute, supplemented with norepinephrine to achieve a target mean arterial pressure (MAP) greater than 65 mmHg and lactate levels below 2 mmol/l. Dynamic parameters, specifically pulse pressure variation (PPV) with a target of less than 12%, guided the resuscitation process. After 72 hours (T2), blood samples were recollected to reassess CLI (I2) and CXCL10 (C2) levels and to calculate the delta cumulative fluid balance. Statistical analysis was then performed.

Data analysis

Pearson's correlation coefficient (r) and determination coefficient (r^2) were used to assess relationships between variables. Correlation strength was classified as very weak (0.00-0.199), weak (0.20-0.399), moderate (0.40-0.599), strong (0.60-0.799), and very strong (0.80-1.00). Normality was tested using the Shapiro-Wilk test. Pearson's correlation was applied for normally distributed data, while Spearman's correlation was used for non-normally distributed data. Statistical significance was set at $p \leq 0.05$. Data were processed using Microsoft Excel 2021 and SPSS version 29.0 (IBM Japan).

Results

Clinical characteristics

This study included 35 patients with sepsis who were admitted to the ICU of Dr. Wahidin Sudirohusodo Hospital, Makassar. All subjects met the inclusion criteria. The majority of the patients were male (22 patients, 62.9%), while 13 patients (37.1%) were female. Vasopressors were administered to 18 patients (51.4%), while 17 patients (48.6%) did not receive vasopressors. Within the first 72 hours, 24 patients (68.6%) survived, whereas 11 patients (31.4%) did not survive. The mean age of the subjects was 46.97±15.46 years, with the youngest being 20 years old and the oldest 64 years old. The mean body mass index (BMI) was 22.39±2.86 kg/m^2, classified within the normal range. The mean serum albumin level on day 1 was 2.76±0.61 g/dl, and the mean CRP level was 170.07±110.55 mg/l (**Table 1**).

Sepsis parameter analysis

The sepsis parameters were measured on days 1 and 3. The mean CLI on day 1 was 68.42±57.28 mg/dl, which decreased to 44.14±46.43 mg/dl on day 3 (**Table 2**, **Figure 1**). The mean CXCL10 level on day 1 was 47.70±45.47 pg/ml, which decreased to 29.34±28.12 pg/ml on day 3 (**Table 2**, **Figure 1**). The mean cumulative fluid balance on day 3 was 727.88±1538.62 ml (**Table 2**, **Figure 2**).

Correlation between CLI, CXCL10, and cumulative fluid balance

Spearman's correlation test demonstrated a significant correlation between CLI and cumulative fluid balance (p=0.049) (**Table 3**). Similarly, a significant correlation was observed between CXCL10 and cumulative fluid balance (p=0.001) (**Table 3**). The correlation coefficient indicated a positive correlation, meaning that higher CLI and CXCL10 levels were associated with a greater cumulative fluid balance. The correlation strength was weak for CLI and cumulative fluid balance (r=0.395) but strong for CXCL10 (r=0.617) (**Table 3**, **Figure 3**).

Correlation between CLI, CXCL10, and Acute Physiology And Chronic Health Evaluation (APACHE II) score

Spearman's correlation test revealed a significant correlation between CLI and APACHE II scores (p=0.049) among ICU patients. The positive correlation indicated higher CLI levels were associated with higher APACHE II scores, although the correlation strength was weak (r=0.327) (**Table 4**, **Figure 4**). However, no significant correlation was found between CXCL10 and APACHE II scores (p=0.089) (**Table 4**).

Correlation between CLI and SOFA score

Spearman's correlation test showed no significant correlation between CLI and SOFA score on day 1 (p=0.087). However, on day 3, a significant correlation was observed between CLI and SOFA score (p=0.008), indicating that higher CLI levels were associated with higher SOFA scores. The correlation strength was moderate (r=0.531) (**Table 5**, **Figure 5**).

Correlation between CXCL10 and SOFA score

Spearman's correlation test indicated no significant correlation between CXCL10 and SOFA score on day 1 (p=0.288). However, on day 3, a significant correlation was found between CXCL10 and SOFA score (p=0.012). This positive correlation suggested that higher CXCL10 levels were associated with higher SOFA scores, with a moderate correlation strength (r=0.502) (**Table 6**, **Figure 6**).

Comparison of CLI, CXCL10, APACHE II, and SOFA scores between surviving and non-surviving patients

An independent t-test revealed a statistically significant difference in CLI levels between the surviving and non-surviving groups within 72 hours (p=0.021). The mean CLI level in the surviving group was 53.57±54.07 mg/dl (24 patients), while in the non-surviving group, it was 100.84±52.40 mg/dl (11 patients). A statistically significant difference was also found in APACHE II scores (p=0.048), with the surviving group having a mean APACHE II score of 11.46±4.16, while the non-surviving group had a mean score of 13.45±1.57 (**Table 7**, **Figure 7**).

However, no statistically significant differences were observed in CXCL10 levels (p=0.234) or SOFA scores (p=0.350) between the surviving and non-surviving groups. The mean CXCL10 level was 41.43±37.08 pg/ml in the surviving group and 61.39±59.74 pg/ml in the non-surviving group. Similarly, the mean SOFA score was 6.58±2.53 in the surviving group and 7.36±1.43 in the non-surviving group (**Table 7**, **Figure 7**).

Summary of findings

This study demonstrated that CLI and CXCL10 levels decreased from day 1 to day 3 in septic patients admitted to the ICU. Higher CLI and CXCL10 levels were significantly associated with increased cumulative fluid balance. Additionally, CLI levels correlated significantly with APACHE II and SOFA scores, particularly on day 3. CXCL10 showed a significant correlation with SOFA scores on day 3 but not with APACHE II scores. Furthermore, CLI and APACHE II scores were significantly higher in non-surviving patients compared to survivors, while no significant differences were found in CXCL10 and SOFA scores between the two groups. These findings suggest that CLI and CXCL10 are potential indicators of disease severity and prognosis in septic patients.

Discussion

Subject characteristics

This study included 35 patients with sepsis admitted to the ICU of Dr. Wahidin Sudirohusodo Hospital, Makassar. All subjects met the inclusion criteria, with a higher proportion of male patients (62.9%) than females (37.1%) (**Table 1**). Similar findings were reported by Abhinandan et al., (19) demonstrating male predominance in sepsis cases. Sepsis affects all age groups, and in this study, the youngest patient was 20 years old, while the oldest was 64 years old, with an average age of 46.97 years (**Table 1**). The predominance of male patients, particularly in the fourth and fifth decades, aligns with the findings of Abhinandan et al.. (19)

During the study period, 11 patients (31.4%) died within 72 hours, while 24 (68.6%) survived (**Table 1**). According to a study by Hu C et al., (20) sepsis-related mortality was commonly associated with septic shock and acute kidney injury, accompanied by increased SOFA and APACHE II scores. Sepsis is a medical emergency that requires immediate intervention and can originate from infections in various body sites, with the lungs, urinary tract, abdomen, and pelvis being the most common sources.

Sepsis is typically caused by bacterial infections, though viral and fungal infections can also contribute. Several risk factors play a role in sepsis incidence, including age, sex, race, comorbidities, genetics, corticosteroid therapy, chemotherapy, and obesity. (20) In this study, the mean BMI was 22.39 (normal) (**Table 1**), which did not align with obesity as a risk factor for sepsis. This suggests that other factors besides BMI may have contributed to sepsis in the study population.

CLI, CXCL10, and cumulative fluid balance delta

Our findings indicated a decrease in CLI and CXCL10 levels from day 1 to day 3 among 24 surviving patients. The mean CLI level decreased from 68.42±57.28 on day 1 to 44.14±46.43 on day 3, while CXCL10 levels declined from 47.70±45.74 on day 1 to 29.34±28.12 on day 3 (**Table 2**, **Figure 1**). This reduction suggests clinical improvement in ICU-admitted septic patients who survived beyond 72 hours. In contrast, patients whose CLI and CXCL10 levels were not assessed on day 3 did not survive. Clinical improvement in sepsis was achieved through standardized treatment and monitoring in the ICU, which not only results in clinical stabilization but also a measurable reduction in CLI and CXCL10 levels.

A study by Cordemans et al. (13) suggested that CLI was a parameter for capillary leakage, as increased vascular permeability due to systemic inflammation was associated with high CRP levels and hypoalbuminemia. Previous research has established CLI as a prognostic tool, aiding in optimizing fluid resuscitation strategies to improve patient outcomes, reduce ICU length of stay, and facilitate earlier recovery. (17)

Similarly, prior clinical studies have demonstrated significantly elevated plasma CXCL10 levels in septic patients, with plasma CXCL10 concentration correlating with disease severity. (9) Punyadeera et al. reported that high plasma CXCL10 levels predicted progression from sepsis to septic shock in adults. (9)

The mean cumulative fluid balance delta in this study was 727.88±1538.62 ml (**Table 2**, **Figure 2**), reflecting variability in fluid administration. This variation may be attributed to differences in fluid management strategies or patient-specific clinical conditions. Fluid resuscitation was guided by real-time PPV monitoring to assess fluid responsiveness, supplemented with norepinephrine to maintain MAP≥65 mmHg and lactate<2 mmol/l. Siddal E et al. (5) noted that fluid resuscitation increased intravascular volume, thereby improving blood pressure and kidney function. However, excessive fluid resuscitation can exacerbate systemic edema, increase effusions, and worsen pulmonary, intestinal, and muscle edema. (5)

Correlation of CLI and CXCL10 with cumulative fluid balance delta

A significant positive correlation was found between CLI levels on day 3 and cumulative fluid balance delta (p=0.049) (**Table 3**), suggesting that capillary leakage necessitated additional fluid therapy, leading to increased cumulative fluid balance. This correlation highlighted the severity of systemic inflammation and its impact on fluid retention and volume status.

A study by Palacious MP et al. (17) found that CLI was a reliable predictor of poor outcomes in septic shock patients. Additionally, Ade S. et al. (15) reported that CRP levels peaked at 36-50 hours post-inflammation, potentially coinciding with peak albumin leakage, contributing to increased intravascular-to-interstitial albumin transfer.

CXCL10 levels on day 3 also showed a significant positive correlation with cumulative fluid balance delta (p=0.001) (**Table 3**), indicating that elevated CXCL10 levels (a marker of capillary leakage) were associated with increased cumulative fluid balance, reflecting fluid accumulation and worsening clinical conditions. CXCL10 is an inflammatory marker linked to increased capillary permeability and fluid imbalance.

A study by Xie et al. (10) in an expanded cohort (35 subjects) demonstrated elevated levels of pro-inflammatory cytokines, particularly CXCL10, in the acute phase of sepsis. Monocytes in the study subjects exhibited an increased capacity for CXCL10 production, highlighting its potential role in systemic capillary leakage syndrome initiation.

CLI (day 3) and CXCL10 (day 3) both correlated with cumulative fluid balance delta (r=0.395 and r=0.617, respectively) (**Table 3**, **Figure 3**). These findings indicated that CLI and CXCL10 contributed to fluid overload in septic patients, with CXCL10 exerting a more pronounced effect. Therefore, strict monitoring and management of fluid status are crucial in patients exhibiting elevated CLI and CXCL10 levels.

Correlation of CLI and CXCL10 with APACHE II on day 1

CLI levels on day 1 were significantly correlated with APACHE II scores (p=0.049) (**Table 4**), indicating that higher CLI levels were associated with higher APACHE II scores, reflecting increased disease severity. However, this correlation was weak (r=0.327) (**Table 4**, **Figure 4**), suggesting that factors beyond capillary leakage influenced disease severity.

In contrast, CXCL10 levels on day 1 did not significantly correlate with APACHE II scores (p=0.292) (**Table 4**), implying that CXCL10 was not a reliable marker of disease severity as measured by APACHE II. This aligned with findings by Hachem H et al., (21) who reported that plasma CXCL10 levels declined sharply from 9183 pg/ml to 483 pg/ml by day 3 and day 14 post-hospitalization.

Correlation of CLI and CXCL10 with SOFA

CLI levels on day 3 were significantly correlated with SOFA scores (p=0.008) (**Table 5**), suggesting that increased CLI levels corresponded to higher SOFA scores, reflecting systemic organ dysfunction. This moderate correlation (r=0.531) (**Table 5**, **Figure 5**) indicated a clinically relevant relationship between CLI and sepsis-related organ failure.

CXCL10 levels on day 3 also significantly correlated with SOFA scores (p=0.012) (**Table 6**), indicating that elevated CXCL10 levels correspond to worsening organ dysfunction. This finding underscored the role of CXCL10 in capillary leakage and systemic inflammation progression.

Overall, these results suggested that CLI and CXCL10 were valuable biomarkers for assessing sepsis severity and prognosis, highlighting the need for close monitoring and tailored fluid management strategies in ICU settings.

The comparison of CLI, CXCL10, SOFA, and APACHE II scores on day 1 between the surviving and non-surviving groups within 72 hours

The study findings indicated that CLI was significantly higher in non-survivors (100.84±52.40) (**Table 7**, **Figure 7**), reinforcing the role of capillary leakage as a crucial determinant of mortality. This aligned with Moguel et al., (21) who identified CLI as a reliable predictor of poor outcomes in severe sepsis and septic shock, with a cutoff value of 85.5 demonstrating good sensitivity and specificity for mortality prediction. CLI, when used alongside APACHE II and SOFA, enhances early risk stratification and prognostic accuracy in septic patients.

Despite being a marker of systemic inflammation and endothelial dysfunction, CXCL10 levels (61.39±59.74) (**Table 7**, **Figure 7**) in non-survivors were not statistically correlated with 72-hour survival. High variability in values and limited sample size may have influenced this outcome. Previous studies, such as those by Punyadeera et al., (9) reported significantly elevated CXCL10 plasma concentrations in sepsis, correlating with disease severity and progression to septic shock, further supporting its role as an inflammatory marker rather than a direct mortality predictor. SOFA scores did not show a statistically significant difference between groups, though slightly higher in non-survivors. This suggested that early SOFA assessment lacked sufficient sensitivity to distinguish survivors from non-survivors within 72 hours. Conversely, higher APACHE II scores in non-survivors reinforced its utility as a prognostic indicator. Metha et al. (22) found that APACHE II provided superior mortality prediction compared to SOFA, while Thakur et al. (23) reported comparable accuracy between both scores in surgical sepsis cases. However, APACHE II demonstrated higher specificity, making it a more reliable predictor of in-hospital mortality. Overall, CLI and APACHE II emerged as significant prognostic parameters, distinguishing survivors from non-survivors, whereas CXCL10 and SOFA lacked specificity for early mortality prediction. Integrating CLI and APACHE II in ICU settings can improve early risk stratification and guide clinical decision-making in sepsis management.

Conclusion

This study highlights the significant correlation between CLI, CXCL10, and cumulative fluid balance in septic ICU patients. The findings suggest that higher CLI and CXCL10 levels are associated with increased fluid retention, reflecting systemic inflammation and disease severity. The observed reduction in these biomarkers among survivors further supports their potential role in prognosis. Additionally, the correlation between CLI, CXCL10, and APACHE II scores underscore their predictive value in sepsis management. Future research should explore targeted interventions to modulate these markers, optimizing patient outcomes through personalized fluid resuscitation strategies.

Table 1. Clinical characteristics based on frequency (n=35)

Variable	Variable group	Result
Gender (%)	Male	22 (62.9)
	Female	13 (37.1)
Patient outcome (<72 hours), n (%)	Survivor	24 (68.6)
	Non-Survivor	11 (31.4)
Postoperative status, n (%)	Yes	20 (57.1)
	No	15 (42.9)
Age (years), mean±SD		46.97±15.46
BMI (kg/m²), mean±SD		22.39±2.86
Albumin on day 1 (g/dl), mean±SD		2.76±0.61
CRP on day 1 (mg/l), mean±SD		170.07±110.55

Legend: SD=standard deviation; BMI=body mass indeks; CRP=C-reactive protein.

Table 2. Mean CLI, CXCL10, and cumulative fluid balance delta

Variable	n	Mean±SD
CLI day 1 (mg/dl)	35	68.42±57.28
CLI day 3 (mg/dl)	24	44.14±46.43
CXCL10 day 1 (pg/ml)	35	47.70±45.47
CXCL10 day 3 (pg/ml)	24	29.34±28.12
Cumulative fluid balance day 3 (ml)	24	727.88±1538.62

Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; SD=standard deviation.

Table 3. Correlation between CLI and CXCL10 with cumulative fluid balance delta

Variable	n	r	95% CI	p
CLI day 3 (mg/dl) and cumulative fluid balance delta (ml)	24	0.395	-0.023 – 0.695	0.049*
CXCL10 day 3 (pg/ml) and cumulative fluid balance delta (ml)	24	0.617	0.273 – 0.821	0.001*

Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; CI=confidence interval.
*p-value significant at p<0.05 using Spearman's test.

Table 4. Correlation between CLI and CXCL10 with APACHE II score on day 1

Variable	n	r	95% CI	p
CLI (mg/dl) and APACHE II	35	0.327	-0.017 – 0.602	0.049*
CXCL10 (pg/ml) and APACHE II	35	0.292	-0.056 – 0.577	0.089

Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; APACHE II=Acute Physiology And Chronic Health Evaluation; CI=confidence interval.
*p-value significant at p<0.05 using Spearman's test.

Table 5. Correlation between CLI and SOFA

Variable	n	r	95% CI	p
CLI (mg/dl) and SOFA day 1	35	0.294	-0.054 – 0.587	0.087
CLI (mg/dl) and SOFA day 3	24	0.531	0.150 – 0.774	0.008*

Legend: CLI=capillary leak index; SOFA=Sequential Organ Failure Assessment; CI=confidence interval.
*p-value significant at p<0.05 using Spearman's test.

Table 6. Correlation between CXCL10 and SOFA

Variable	n	r	95% CI	p
CXCL10 (pg/ml) and SOFA day 1	35	0.185	-0.168 – 0.496	0.288
CXCL10 (pg/ml) and SOFA day 3	24	0.502	0.111 – 0.758	0.012*

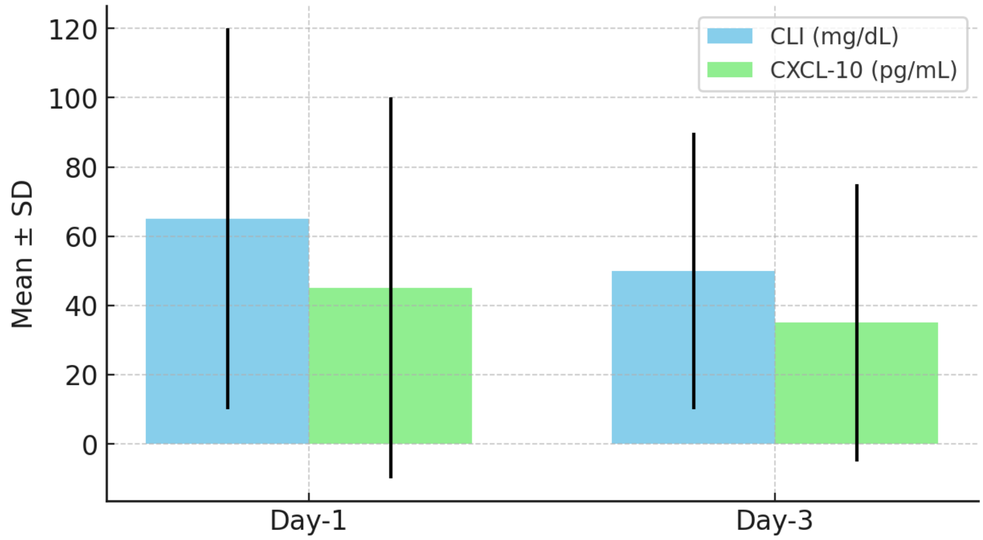
Legend: CXCL10=C-X-C motif chemokine ligand 10; SOFA=Sequential Organ Failure Assessment; CI=confidence interval.
*p-value significant at p<0.05 using Spearman's test.

Table 7. Comparison of CLI, CXCL10, SOFA, and APACHE II scores on day 1 between survivors and non-survivors within 72 hours

	Outcome<72 hours	n	Mean±SD	p
CLI (mg/dl)	Survivor	24	53.57±54.07	0.021*
	Non-survivor	11	100.84±52.40	
CXCL10 (pg/ml)	Survivor	24	41.43±37.08	0.234
	Non-survivor	11	61.39±59.74	
APACHE II	Survivor	24	11.46±4.16	0.048*
	Non-survivor	11	13.45±1.57	
SOFA	Survivor	24	6.58±2.53	0.350
	Non-survivor	11	7.36±1.43	

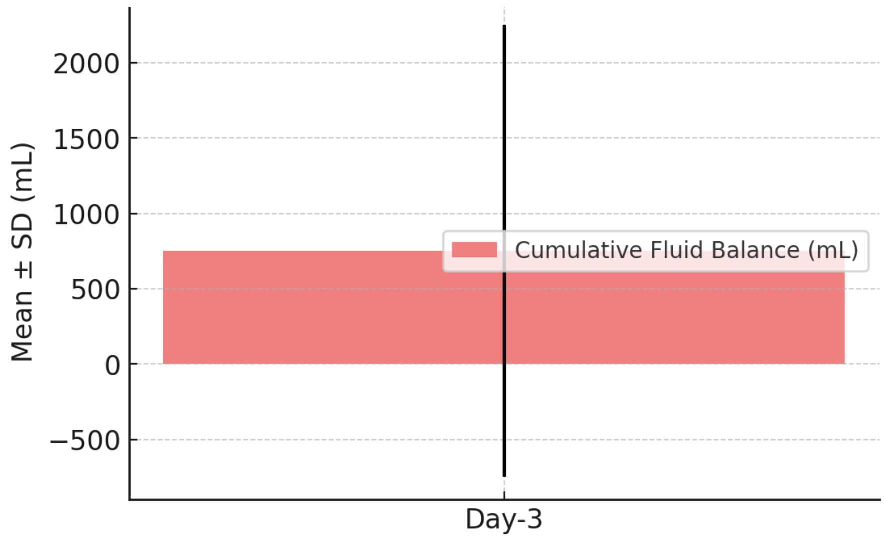
Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; SOFA=Sequential Organ Failure Assessment; APACHE II=Acute Physiology And Chronic Health Evaluation; SD=standard deviation.
*p-value significant at p<0.05 using an unpaired t-test.

Figure 1. Mean CLI and CXCL10 on day 1 and day 3



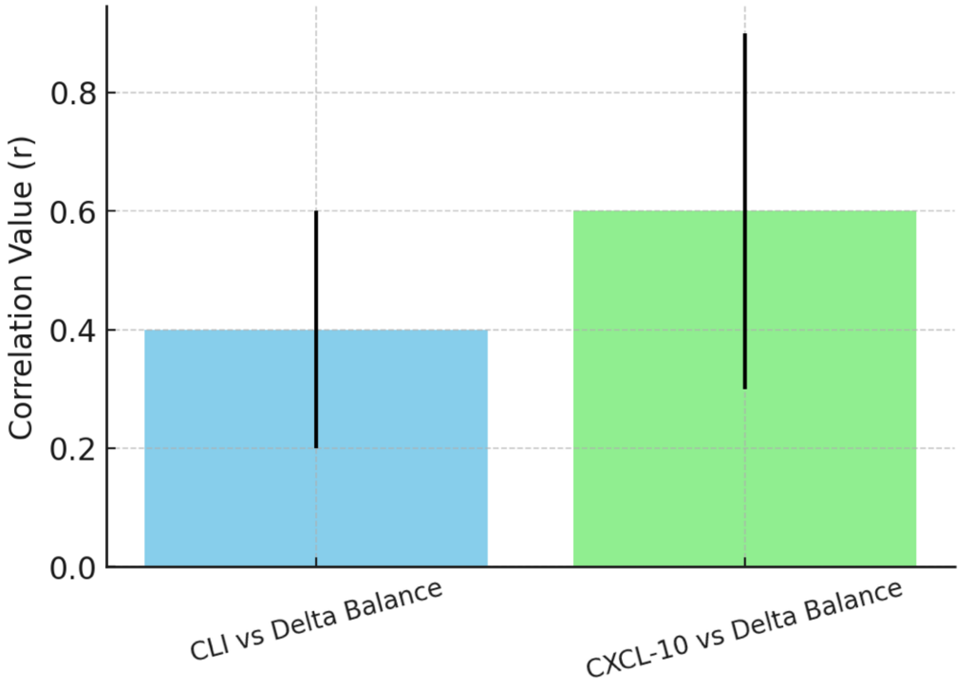
Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; SD=standard deviation.

Figure 2. Cumulative fluid balance on day 3



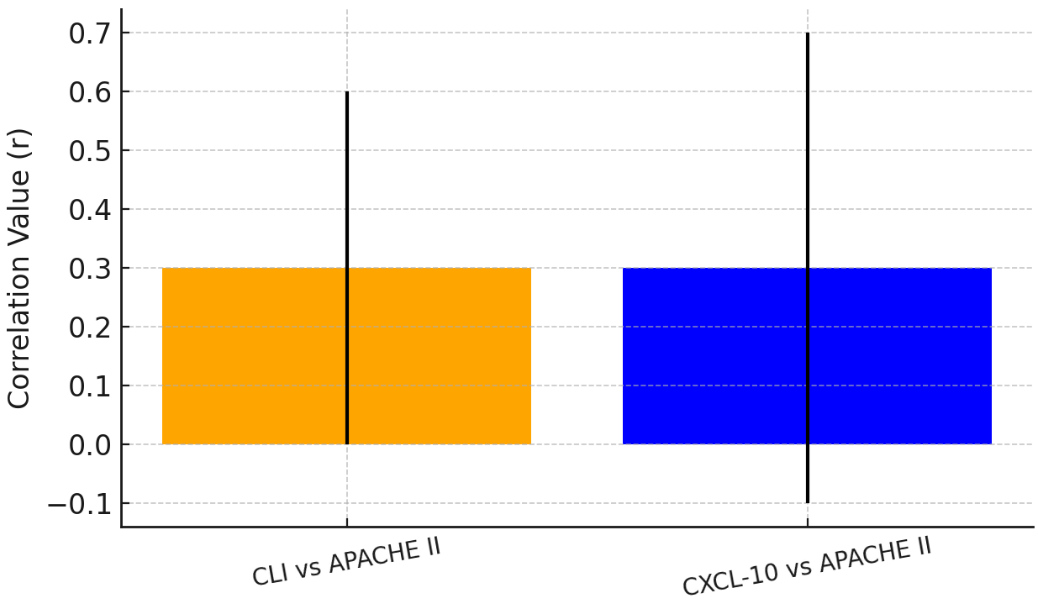
Legend: SD=standard deviation.

Figure 3. Correlation of CLI and CXCL10 with cumulative fluid balance delta



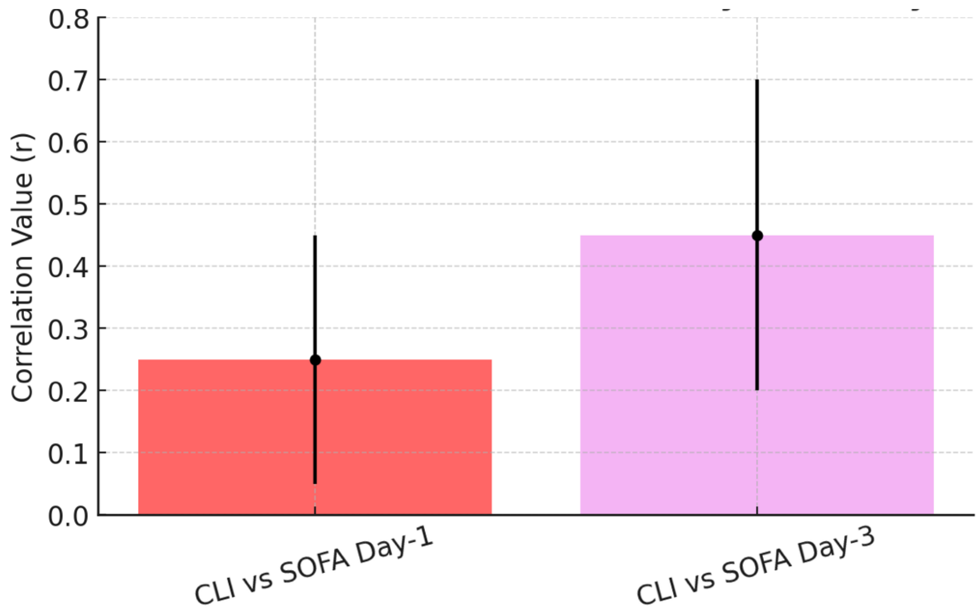
Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10.

Figure 4. Correlation of CLI and CXCL10 with APACHE II score



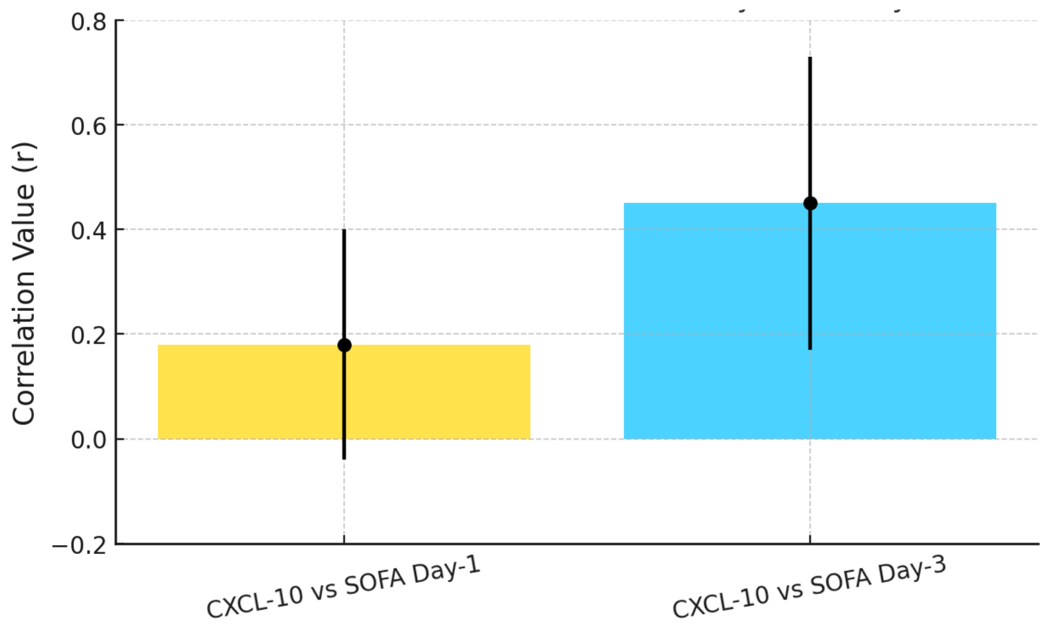
Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; APACHE II=Acute Physiology And Chronic Health Evaluation.

Figure 5. Correlation of CLI with SOFA on day 1 and day 3



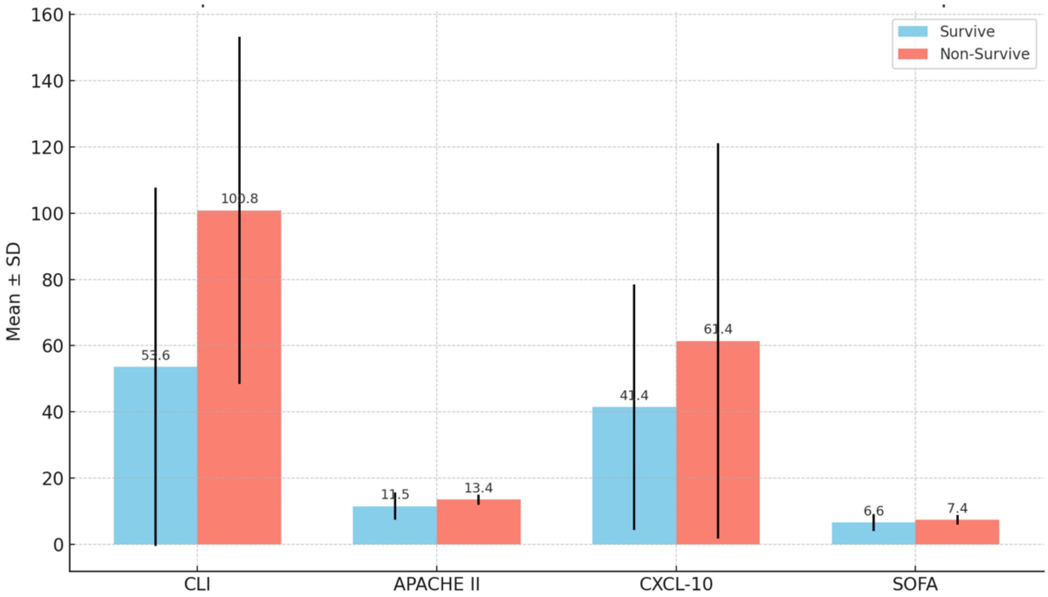
Legend: CLI=capillary leak index; SOFA=Sequential Organ Failure Assessment.

Figure 6. Correlation of CXCL10 with SOFA on day 1 and day 3



Legend: CXCL10=C-X-C motif chemokine ligand 10; SOFA=Sequential Organ Failure Assessment.

Figure 7. Comparison of mean CLI, CXCL10, APACHE II, and SOFA scores based on outcome <72 hours



Legend: CLI=capillary leak index; CXCL10=C-X-C motif chemokine ligand 10; APACHE II=Acute Physiology And Chronic Health Evaluation; SOFA=Sequential Organ Failure Assessment; SD=standard deviation.

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